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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :

Bertram CEZANNE et al.

Examiner: Joseph R. Kosack

Serial No.: 10/519,356

Group Art Unit: 1626

Filed: December 28, 2004

Title: 2-(PHENYL)-2H.PYRAZOLE-3-CARBOXYLIC ACID-N-4-(THIOXO-HETEROCYCLYL)-PHENYL-AMIDE DERIVATIVES AND CORRESPONDING IMINO-HETEROCYCLYL DERIVATIVES AND RELATES COMPOUNDS FOR USE AS INHIBITORS OF THE COAGULATION FACTORS XA AND/OR VIIA FOR TREATING THROMBOSES

PETITION OF THE RESTRICTION REQUIREMENT UNDER 37 C.F.R. §1.181

TECHNOLOGY CENTER 1600
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is a petition requesting the Commissioner, through the Honorable Group Director, to reverse the Examiner's decision in instituting a Restriction based on single compounds and denying extension of the search beyond the elected invention.

Statement of Facts

In the Office Action of January 17, 2006, the Examiner instituted a Restriction Requirement asserting that the claims did not form a general inventive concept under PCT Rule 13.1. The Examiner asserted that the variable groups in the claims were widely divergent and did not permit a "precise listing of inventive groups." Instead, the Examiner listed 9 exemplary groups. In particular, Groups I-VI were each directed to claims 1-25 and 27-30 in part and were

each defined by a single compound of applicants' formula I as follows:

Group I: N-[4-(2-iminopyrrolidin-1-yl)phenyl]-2-(3-aminomethyl-phenyl)-5-trifluoromethyl-2H-pyrazole-3-carboxamide;

Group II: N-[4-(2-thioxopyrrolidin-1-yl)phenyl]-2-(3-aminocarbonyl-phenyl)-5-trifluoromethyl-2H-pyrazole-3-carboxamide;

Group III: N-[3-chloro-4-(2- thioxopyrrolidin-1-yl)phenyl]-2-(3- aminocarbonyl-phenyl)-5-trifluoromethyl-2H-pyrazole-3-carboxamide;

Group IV: N-[4-(2-iminopyrrolidin-1-yl)phenyl]-2-(3- aminocarbonyl-phenyl)-5-trifluoromethyl-2H-pyrazole-3-carboxamide;

Group V: N-[4-(2-methoxyiminopyrrolidin-1-yl)phenyl]-2-(3- aminocarbonyl-phenyl)-5-trifluoromethyl-2H-pyrazole-3-carboxamide; and

Group VI: N-[3-methyl-4-(2-methoxyiminopyrrolidin-1-yl)phenyl]-2-(3- aminocarbonyl-phenyl)-

The remaining "exemplary groups" were directed to methods of preparation (Group VII), methods of use (Group VIII), and kits containing compounds of applicants' formula I.

In making the restriction, the Examiner asserted that the compounds recited in the claims lacked unity of invention under PCT Rules 13.1 and 13.2 because the compounds allegedly lacked "a significant structural feature qualifying as the special technical feature that defines a contribution over the prior art." The Examiner argued that the compounds contained a structure which was said to not be a contribution over the prior art, citing WO 98/28269.

Applicants responded in an Election filed February 17, 2006 and elected Group I, with traverse. In doing so, applicants first asked for clarification on the scope of the subject matter of Groups I-VI. Applicants argued that it was unclear whether the scope of examination for each of these groups would be limited to a single compound or whether the scope will include other structurally related compounds. Applicants stated that they assumed the latter, but then indicated it was still unclear as to what scope of structurally related compounds would be examined for each group.

Applicants further argued that Groups I-VI did not lack unity of invention because the compounds used to define these Groups were structurally very similar. Applicants argued that

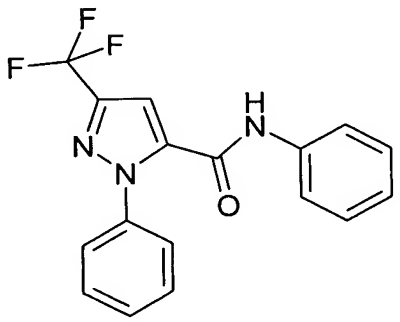
these compounds do not have variable groups with widely divergent meanings, as alleged by the Examiner.

Applicants further argued that groups I-VI all stem from a class of related compounds disclosed in the specification as having the same general set of properties and utilities and did not lack unity of invention.

Applicants cited section (f) of Annex B of the Administrative Instructions under the PCT, Part I, which is directed to unity of invention under Rules 13.1 and 13.2. Section (f) indicates that where a "Markush Grouping" is for alternatives of chemical compounds, they *shall* be regarded as being of a similar nature, and meeting the requirement of a same or corresponding technical feature, provided that they fulfill a specific set of criteria. Applicants argued that the compounds identified in Groups I-VI did fulfill the criteria of §(f) of Annex B because:

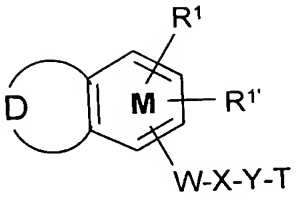
(A) The compounds of Groups I-VI *have a common property or activity* since they all possess inhibitory activity against the activated coagulation protease, factor Xa.

(B)(1) The compounds of Groups I-VI *have a common structural element* since they all possess a significant core structure as outlined below.



As for Groups VII-IX, applicants argued that these Groups constituted part of the same invention as Groups I-VI, citing §(e) of Annex B.

The Examiner then issued an Office Action on April 20, 2006. In the Office Action, the Examiner stated that the scope of the invention would be limited to the applicants' formula I:



in which D was absent, M is a phenyl ring, W is pyrazole attached to the M ring via its 1-position, R^1 is $-CH_2NH_2$ attached to the meta position of the pyrazole ring, X is CONH attached to the 5-position of the pyrazoles ring, and Y and T are as defined in claim 1.

The Examiner did not respond to applicants' arguments directly but stated that the arguments were unpersuasive. The Examiner further argued that the withdrawn subject matter contained varying functional groups that were asserted to be of recognized chemical diversity by the separate classification in the USPTO classification system. Also, the Examiner argued that the non-elected subject matter would have a "different core structure than that listed above" and therefore would have a different special technical feature and would lack unity of invention. The Examiner further indicated in that Office Action that the examined scope of the compound claims was allowable (see the statement on page 9 of the Office Action that claims 1-3, 6-31 and 33-44 are free of the prior art).

In the Reply filed applicants again traversed the Restriction and requested the Examiner to expand the scope of examination. Applicants argued that Examiner's failure to extend the scope of was improper and violated the procedure, as set forth in the MPEP, for examination following an election of species and for examination of Markush claims.

The applicant noted the application was a US national phase of a PCT application, and that unity of invention for PCT applications fell under PCT Rule 13. Further, the applicants argued that the claims were Markush claims, and that requirements for Markush claims the requirements under Rule 13.2 for unity of invention were met when: (1) the alternatives in the Markush claim have a common property or activity, and (2) either (a) the compounds share a significant structural element, or (b) the compounds all belong to a recognized class of chemical compounds. Applicants also cited See also MPEP §1850 (III)(B). In addition, applicants argued that Annex B of the Administrative Instructions under the PCT, entitled "Unity of Invention,"

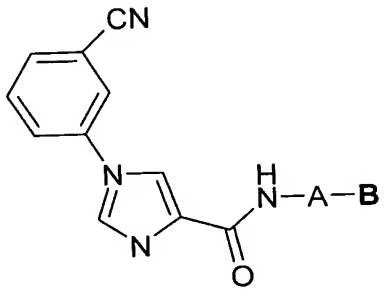
stated that merely because members of the Markush claim can be differently classified does not justify a finding of lack of unity of invention. See section (f)(iv) of Annex B.

Applicants argued that claimed Markush group satisfied the requirements of Rule 13.2 beyond the scope examined by the Examiner. For example, when M is phenyl and D is absent, all of the compounds have a phenyl ring as a core structure with up to three substituents.

Moreover, applicants argued that the original Restriction Requirement divided the compound claims based on individual compounds. As a result, the Restriction was actually an election of species requirement. In accordance with MPEP §809.02(c), upon determination that the elected species is allowable, as in the case here, examination should be extended to other species. Thus, the Examiner's decision to arbitrarily stop examination after examining a narrow scope of the claim was contrary to the procedure set forth MPEP §809.02(c).

Furthermore, applicants argued that US law, specifically 35 USC §121, does not permit restriction within a single claim (except in the case of an improper Markush rejection) citing *In re Weber et al.*, 198 USPQ 328 (1978).

In the Final Office Action issued September 15, 2006, the Examiner maintained the Restriction Requirement. The Examiner argued that the core structure of applicants' formula I was a conjugated 6-membered ring structure with a ring structured attached thereto. Further, the Examiner argued that such a structure did not define a technical feature that makes a contribution over the prior art in light of the following compound taught by WO 98/28269:



Additionally, the Examiner argued that since all of the variable groups in applicants' formula I could be different, unity of invention was lacking. In support, the Examiner cited

Example 24 of Chapter 10 of the International Search and Preliminary Examination Guidelines.

The Examiner also pointed out the Chapter 800 does not apply to National Stage applications under 35 USC 371 and that lack of unity of invention is handled under 35 USC 372, not 35 USC 121.

Summary of Argument in Support of Reversal of Denial to Extend the Search

Applicants maintain that the initial Restriction Requirement was improper since it required applicant to elect a single invention define by a single compound. This is effectively the same as an election of species requirement which is covered by MPEP §809.02(c). However, as the Examiner noted Chapter 800 of the MPEP does not apply to National Stage applications under 35 USC 371. The Examiner has cited no support under PCT Rule 13 for instituting an election of species requirement. Thus, the Restriction should be withdrawn and the Groups of the Restriction clarified.

As applicants argued in their Replies, Groups I-VI identified by the Examiner do not lack unity of invention because the compounds used to define these Groups are structurally very similar. The compound identified in Group I and the compound in Group IV differ only by a single substituent, i.e. 3-aminomethyl vs. 3-aminocarbonyl. Similarly, the compounds in groups II, IV, and V differ only by one substituent on the pyrrolidinyl ring, i.e., thioxo vs. imino vs. methoxyimino. The compounds of Groups II and III also differ by only a single substituent, i.e. a 3-chloro substituent on a phenyl ring. Furthermore, Groups V and VI differ by only a single substituent, i.e. a methyl substituent on a phenyl ring. Each of the compounds used to define Groups I-VI possess a pyrazole ring which is substituted by two phenyl groups, a trifluoromethyl group, and a carboxamide group. The Examiner has not shown why such Groups lack unity of invention under PCT Rule 13, especially in light of section (f) of Annex B of PCT Administrative Instructions, discussed further below. Thus, for this reason also, the Restriction should be withdrawn and the Groups of the Restriction clarified.

Additionally, applicants maintain that the manner in which the Examiner has applied the Restriction under PCT Rule 13 is improper. The Examiner argues that, pursuant to PCT Rule

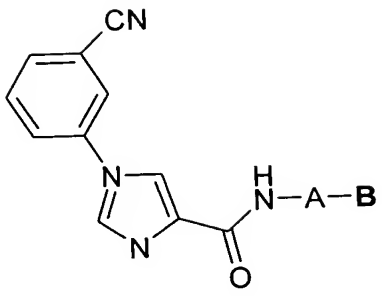
13.2, the compounds of applicants' formula I do not possess a special technical feature which defines a contribution over the prior art. In support of this assertion, the Examiner cited the compound disclosed by WO 98/28269. However, this assertion fails to take into account: (1) how the PCT Administrative Instructions define "special technical feature," as that term is used in PCT Rule 13.2, with respect to Markush Practice, and (2) the language of applicants' dependent claims.

Section (f) of Annex B expressly states that in the special situation of Markush Practice "the special technical features as defined by Rule 13.2" shall be considered to be met when the Markush alternatives are of a similar nature. Annex B further states that, when the Markush group is for alternatives of chemical compounds, the requirement of similar nature is met when: (a) all alternatives have a common property or activity, and (b) a common structure is present, i.e., a significant structural element is shared by all the alternatives. See section(f)(i). Also, the criteria of "significant structural element" are met when the compounds share a common chemical structure which occupies a large portion of their structures. See section (f)(ii)). Annex B does not necessitate that this large portion be distinctive over the prior art.

The Examiner has never applied the test set forth section (f) of Annex B to applicants' claims. Thus, the Examiner has not demonstrated that Restriction is justified under PCT Rule 13 as to all of applicants' Markush compound claims.

The compounds of applicants' Formula I have a common property or activity since they all possess inhibitory activity against the activated coagulation protease, factor Xa. Moreover, applicants' dependent claims clearly recite compounds that all share a significant structural element that occupies a large portion of their structures. See, for example, claims 34, 45 and 46 (and the claims dependent thereon) which recite that D is absent, M is phenyl, and W is pyrazolediyl. The arguments in support of the Restriction Requirement provide no rational as to why these claims do not satisfy unity of invention pursuant to Rule 13.2 and section (f) of Annex B.

As noted above, the Examiner cites the disclosure by WO 98/28269o f the following compound in support of the Restriction:



This compound has an imidazole group attached to a phenyl ring. This compound does not support a Restriction under Rule 13.2 and Annex B with respect to applicants' claims 34, 45 and 46 and the claims dependent thereon.

Further, the Examiner reference to Example 24 of Chapter 10 of the International Search and Preliminary Examination Guidelines is not relevant to applicants' claims 34, 45 and 46 and the claims dependent thereon. As mentioned, applicants' claims 34, 45 and 46 and the claims dependent thereon recite hat D is absent, M is phenyl, and W is pyrazolediyl.

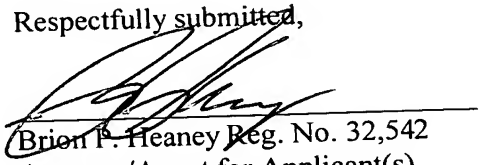
Regarding Groups VII-IX, applicants have argued that these Groups constituted part of the same invention as Groups I-VI, citing §(e) of Annex B. The Examiner has never refuted this argument. It is noted that the Examiner has included the claims of Groups VII and VIII in the examination. However, applicants respectfully submit that the Restriction Requirement as to kit claim 32 of Group XI should also be withdrawn. The Examiner has presented no reason why the kit claim should not be examined pursuant to section (e) of Annex B since the kit would be an apparatus specifically designed for carrying out the methods of treatment of the invention.

Conclusion

For the forgoing reasons, Applicants request reversal of the Examiner's Restriction Requirement to at least clarify the Groups of the Restriction, and that examination be extended at least encompass the subject matter of applicants' formula I in which D is absent, M is phenyl, and W is pyrazolediyl.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



Brion P. Heaney Reg. No. 32,542
Attorney/Agent for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: **MECK-2952**

Date: September 27, 2006